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An individual-based model of rabbit viral haemorrhagic disease in European wild rabbits (*Oryctolagus cuniculus*)

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Abstract

We developed an individual-based model of Rabbit Viral Hemorrhagic Disease (RVHD) for European wild rabbits (*Oryctolagus cuniculus* L.), representing up to 1000 rabbits in four hectares. Model output for productivity and recruitment matched published values. The disease was density-dependent and virulence affected outcome. Strains that caused death after several days produced greater overall mortality than strains in which rabbits either died or recovered very quickly. Disease effect also depended on time of year. We also elaborated a larger scale model representing 25 km^2 and 100,000+ rabbits, split into a number of grid-squares. This was a more traditional model that did not represent individual rabbits, but employed a system of dynamic equations for each grid-square. Disease spread depended on probability of transmission between neighboring grid-squares. Potential recovery from a major population crash caused by the disease relied on disease virulence and frequency of recurrence. The model's dependence on probability of disease transmission between grid-squares suggests the way that the model represents the spatial distribution of the population affects simulation. Although data on RVHD in Europe are lacking, our models provide a basis for describing the disease in realistic detail and for assessing influence of various social and spatial factors on spread.

Keywords: Individual-based models; Rabbit viral hemorrhagic disease; Rabbits

1. Introduction

Rabbit Viral Hemorrhagic Disease (RVHD) was first detected in China in 1984 (Liu et al., 1984; Rodák et al., 1990a) in domestic rabbits (*Oryctolagus cuniculus* L.). The virus, a calicivirus, is fatal in the early stages of an epizootic (Smid et al., 1989, 1991; Ohlinger et al., 1990; Parra and Prieto, 1990). It causes lesions including hemorrhage, gross swellings in the major organs especially liver and lungs, and to a lesser extent in the kidneys and spleen. Aerosol droplet infection is probably the transmission method, with incubation time of around 20–48 h, after which death may follow rapidly (Xu and Chen, 1989; Nowtny

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et al., 1993). In some cases, the ante-mortem morbidity period can be up to 2 weeks.

RVHD has spread rapidly since 1984, appearing in former Czechoslovakia in 1987 (Smid et al., 1991) and spreading to Germany, Poland, Italy, France and Spain a year later (Argüello et al., 1988; Smid et al., 1991). It has been reported in Austria (Kolbl et al., 1990), Belgium (Peeters et al., 1990), UK (Fuller et al., 1993; Chasey, 1994), and Mexico (Gregg and House, 1989). In most countries, the impact of the disease has been mainly upon domestic and commercial rabbits, but RVHD has also had a serious effect on free-living populations. In southern Spain, for example, 60 + % of the wild rabbit population died in the initial epizootic (Blanco and Villafuerte, 1993; Villafuerte et al., 1994; Gortazar, 1997; Fa et al., 1999).

Although studies on RVHD epizootiology in Australian rabbit populations are now emerging (Bowen and Read, 1999; Pech and Hood, 1999; Saunders et al., 1999; Pech et al., 1994), the role of RVHD in rabbit population crashes in Europe is still unclear. While gathering information on the impact of the disease and its likely effect in the future is of prime importance, a complementary approach is the application of theoretical epizootiology (Anderson and May, 1979a,b). Epizootiological models on myxomatosis and rabbits have increased understanding of the co-evolution of the virus and its host and of the role of disease in rabbit population dynamics (May, 1985; Dwyer et al., 1990). Krebs (1986) considers the rabbit/myxomatosis system to be the most widely quoted example of host-disease co-evolution in the literature. This is largely due to May (1985). The general epizootiological model of Anderson and May (1979a) can be expressed as:

$$\frac{dS}{dt} = rN - \beta SI - mS, \tag{1}$$

$$\frac{dI}{dt} = \beta SI - (m + \delta + \gamma)I, \tag{2}$$

$$\frac{dR}{dt} = \gamma I - mR, \tag{3}$$

where S, I and R represent the number of susceptible, infected and recovered animals; N is the total number of animals; r is the intrinsic rate of increase of the population; m is the natural mortality rate; β is the rate of transmission of disease; δ is the additional mortality due to disease; and γ is the rate of recovery from disease.

This model may also be expressed in discrete time, thus:

$$S_{t+1} = S_t + [rN_t - \beta S_t I_t - mS_t]\Delta t, \tag{4}$$

$$I_{t+1} = I_t + [\beta S_t I_t - (m + \delta + \gamma)I_t]\Delta t, \tag{5}$$

$$R_{t=1} = R_t + [\gamma I_t - mR_t]\Delta t, \tag{6}$$

where $\Delta t = 1$ is the time step, S_t is the number of susceptible rabbits at time t, S_{t+1} is the number of susceptible rabbits at time $t + 1$, and so on.

Conventional approaches to modeling rabbit population dynamics have encountered difficulties in the estimation of population parameters. Most rabbit models used to date have not specifically combined accurate representation of both population dynamics and disease. Models of disease tend to have rather simple population dynamics (Dwyer et al., 1990), whilst population models do not have detailed simulations of disease (Smith and Trout, 1994). In an attempt to simulate the impact of RVHD on Australian rabbit populations, Barlow and Kean (1998) developed an age-structured, deterministic model, which used demographic data from studies in New Zealand and Australia and epizootiological data from Spain. This model included differences in productivity between age classes, climatic variation, predation, disease virulence and transmissibility, and followed on from previous studies of disease in rabbits (Barlow, 1993a) and other animals (Barlow, 1993b). However, there is no explicit spatial representation, and like Smith and Trout (1994), the model is based on Leslie matrices. Although these models produced a good fit to the wild rabbit population data used to determine the population parameters, they are not able to represent processes of spatial movement, local interactions, and social behavior that may be critical to the dynamics of a disease in a population.

Many of the difficulties and limitations of Leslie matrix models or population-level models in adequately representing a population composed of a number of discrete classes with widely differing responses to variables such as infection, movement

etc. can be addressed by using individual-based models, or IBMs (De Angelis and Gross, 1992). These allow the modeler to have much more flexibility in representing population processes, by tracking all the individuals in a population and deriving births, deaths and other processes directly from the properties of the individuals. In fact the IBM can be considered as the extension of a population projection matrix (as in the Leslie matrix), such that each individual in the population represents an age/sex class of its own (Judson, 1994).

IBMs operate by following a number of simple sets of rules, and new processes can usually be added into the original model without making it any more difficult to perform model simulations. This cannot be said of analytical models; the attractive property of analytic tractability is quickly lost with increasing model complexity. Each process in an IBM can be contained within one set of rules that govern the responses of individuals within any given situation. The population level processes, such as birth and death rates, can be obtained simply by summing over all the individuals represented. In this way, it is theoretically possible to combine a realistic population model with a realistic disease model. Theoretically, there is no limit to the number of processes which can be included, although it is good model design to include only processes and factors that are essential to describe the system. However, the number of attributes that an individual can have in an IBM greatly exceeds that of conventional models. In addition, IBMs are oriented towards the processes modeled, rather than the classes involved. The program can thus be split into routines that cover one process, such as births, as opposed to having a number of distinct equations for each age/sex class or disease status, each containing a number of different processes. This adds greatly to the ease of understanding and implementing the model system.

The IBM can also be used as a first step towards a conventional analytical model. It allows detailed representation of spatial configurations and movements in space (Caswell and John, 1992), so that the effects can be simulated. Study of the results may reveal that simpler analytic models can represent the simulated dynamics with reasonable accuracy.

In this paper, we provide an exploratory approach to modeling RVHD. We concentrate on European populations of wild rabbits, and thus our models' applicability to Australasian populations may be limited. The discussion of the results will focus on the applicability and validity of the various techniques used, rather than on theoretical insights gained into the disease. There are several reasons for this. Firstly, there are very few empirical data on the epizootiology of RVHD in wild rabbit populations in Europe at present, which makes any theoretical treatment at this stage somewhat speculative. Secondly, IBMs such as that reported here, have rarely been applied to epizootiology (although see David et al., 1982).

We develop the paper in two separate phases: (1) an individual-based model of RVHD within a small rabbit population will be described. The role of this model will be to focus on mortality, transmissibility, timing of epizootics, and effects of population density. In particular, spatial aspects of disease spread and transmission will be considered. This model, known as the Spatial Model, provides a realistic description of the population dynamics of a small rabbit population; (2) the next stage is to develop a large-scale model, which represents population states rather than individual rabbits. This model will be derived directly by converting the processes underlying the Spatial Model to the metapopulation level. The role of this model, the Regional Model, will be to look at the recurrence of disease over many years and the spread of the disease over a wide area, and to attempt to identify the long-term population implications of the disease.

2. Results

2.1. The Spatial Model: development

2.1.1. General

This is a spatially explicit mixed stochastic–

deterministic, individual-based model, which represents a population of up to 1000 rabbits in an area of 4 hectares. The rabbits move around a number of 10×10 m grid-squares, interact with other rabbits, and reproduce and die according to a number of simple rules. Disease can be introduced to the system at any point in the annual cycle. The model has a number of user-defined parameters, which control population processes, such as birth and death rates, and the disease parameters, such as virulence, probability of transmission, and time of outbreaks. The rabbits belong to one of five mutually exclusive age/sex classes (Adult Male, Adult Female, Juvenile Male, Juvenile Female, Infant). Rabbits are classed as infants from birth to age 21 days (Webb, 1993), which corresponds to the period in which they are confined to the natal nest. Sex is assigned to rabbits when they become juveniles, in a ratio, which is supplied by the user (JSR, Table 1). Rabbits are juveniles from 22 to 200 days: during this period they cannot breed. Although rabbits are in fact able to breed from as early as 130 days of age in Australia, and can breed in their first season (Gilbert et al., 1987), this is less common in Europe, and breeding success is limited until after 190 days (Smith and Trout, 1994). Juveniles were therefore not allowed to breed in this model; all young born are thus the offspring of any adults present at the start of the annual cycle.

Table 1
User-defined parameters for Spatial Model

	Range
Initial population parameters	
Initial population size (no. of rabbits)	20–400
Initial proportion of Infants	0–1
Initial proportion of Juveniles	0–1
Juvenile sex ratio	0–1
Adult sex ratio	0–1
Number of warrens	4, 8, 16, 24 or 36
Initial distribution of rabbits in warrens	0 = uniform, 1 = random
Maximum number of rabbits per grid-square	0 = uniform (10), 1 = random (5–15)
Initial month of year	0 (January)–11 (December)
Number of iterations	30–365
Population dynamics parameters	
Home range size, for each A/S class	0–5 (grid-squares from home warren)
Mortality rates, for each A/S class	0–1
Monthly probability of pregnancy	0–1
Start and end dates of extra mortality period	0–300
Extra mortality rates, for Adults and Juveniles	0–1
Disease parameters	
Total number of infections	0–15
Probability of death at stages 1–4 of disease	0–1
Probability of transmission of disease	0–1
Time of nth infection	1–355
Number of warrens in nth infection	1-Number of warrens
Number of infected rabbits in each warren	1–15

After the population has been prepared the model proceeds through 365 iterations, each representing 1 day, and giving a model lifetime of 1 year. The model can be started at any month, and the initial composition of the population can be altered, as can the distribution of the rabbits within the grid and the carrying capacity of the landscape. In each daily time step of the model, the various processes, such as Births, Deaths, Movement and Disease, are performed on all rabbits in turn, i.e. all rabbits move, then all rabbits have a risk of mortality. Some of the procedures, such as Dispersal and Births apply only to specific age/sex classes.

Data for the population and disease parameters were obtained from the literature. Estimates of fecundity and survival were taken from Wheeler and King (1985), Gilbert et al. (1987), Williams and Moore (1989), Bell and Webb (1991), Gibb (1993), Rogers et al. (1994) and Smith and Trout (1994). Since accurate data on disease parameters in wild populations were not available, accounts of the disease in captive rabbits were used (Xu and Chen, 1989; Nowtny et al., 1993) as well as the partial data on the disease in wild rabbits in Spain (Villafuerte et al., 1994). Full descriptions

Table 2
Parameters for Regional Model

	Range
Initial population parameters	
Initial population size (no. of rabbits)	20–400
Initial proportion of Infants	0–1
Initial proportion of Juveniles	0–1
Juvenile sex ratio	0–1
Adult sex ratio	0–1
Initial distribution of rabbits in grid-squares	0 = uniform. 1 = small variation, 2 = large variation
Carrying capacity of grid-squares	Uniform or Random, 500–5000 rabbits
Number of years	1–20
Population dynamics parameters	
Probability of emigration, for JM and JF	0–1
Mortality rates, for each A/S class	0–1
Monthly probability of pregnancy	0–1
Fecundity	2–10
Disease parameters	
Total number of infections	0–15
Probability of death at stages 1–4 of disease	0–1
Probability of transmission of disease within grid-square	0–1
Probability of transmission of disease between grid-squares	0–1
Date and year of nth infection	1–355
Number and location of grid-squares in nth infection	1–20
Number of infected rabbits in each warren	1–500

of the parameter values investigated are given in Table 1 and Table 2. Full program source code and documentation (for both models) can be obtained from the authors on request.

2.1.2. Movement and dispersal

Within the 4 ha area, a number of warrens (4, 8, 16, 24 or 36) are placed in a regular pattern. The warrens can all be assigned the same carrying capacity or each warren can be assigned a carrying capacity chosen randomly around a common mean, but the carrying capacity for each warren remains constant throughout the lifetime of the model. Similarly, each of the 10×10 m grid-squares can uniformly contain up to a maximum of 10 rabbits, or can have a randomly assigned capacity of between five and 15 rabbits. Each rabbit has a 'home' warren around which it moves. On each day, a rabbit will occupy one grid-square, interacting only with rabbits also in that grid-square. The rabbits move to a new square each day, within a user-defined home range of a number of squares about the home warren. While rabbits tend to have a daily range larger than 100 m^2 (see Gibb, 1993; Kolb, 1994), in any 1 day it is unlikely that a rabbit will interact with all other rabbits in its own warren, especially when the warren is overcrowded. With the method used in this model, the rabbits will, over time, interact with both the other members of the warren, and rabbits from neighboring warrens. For the simulations used here, the home ranges were as follows (based on Gibb, 1993): Adult Males 25 squares (0.25 ha); Adult Females 9 squares (0.09 ha); Juvenile Males 49 squares (0.49 ha), Juvenile Females 25 squares (0.25 ha), and Infants 1 square (i.e. the home warren square).

To allow for mixing between warrens, and to account for the juvenile dispersal seen in wild rabbits, Juvenile Males and Females are allowed to disperse to other warrens. This is age-dependent: males disperse from the age of 120 days, females from 150 days; males also disperse much more frequently than females (Dunsmore, 1974; Parer, 1982; Webb et al., 1995). In this model, dispersal is also density dependent; only rabbits whose home warren contains more rabbits than the mean for all warrens will disperse.

2.1.3. Reproduction

Reproduction simulates the 30-day pregnancy of rabbits. Females become pregnant according to a deterministic, month-specific probability and then only if there is an adult male available to interact with (i.e. in the same square). The female will be pregnant for 30 days, and will then give

birth to a litter of between two and seven infants (mean litter size in rabbits in continental Europe varies between 3.2 and 4.1, Rogers et al., 1994). The size of the litter is random, but is also density-dependent. If the litter would take the female's warren beyond its carrying capacity, the litter will be density-dependent: as the warren's population approaches carrying capacity, so the probability of pregnancy (for all females in that warren) tends to zero.

As rabbits exhibit post-partum estrous, females become available for mating immediately after giving birth. Seasonality in breeding is user-defined, by setting different probabilities of pregnancy for each month. In the model runs, breeding occurs from December through June. The length of the breeding season is dependent upon climate (both temperature and rainfall) and day length (Bell and Webb, 1991); in parts of Australia, under favorable climatic conditions, breeding can be virtually continuous (Gilbert et al., 1987), while in northern Europe the breeding season can be as short as 3 months (Bell and Webb, 1991; Rogers et al., 1994). In Spain, breeding season has been recorded as lasting from November through to May or June, with a mean duration of 210 days (Rogers et al., 1994).

2.1.4. Natural mortality

For the purposes of the model, all deaths due to predation, starvation, senescence and diseases other than RVHD are treated as natural mortality. To allow for variation in mortality rates with season, a period of extra mortality can be defined if necessary. This extra mortality period can be used to simulate the effects of myxomatosis, which normally occurs in late summer/autumn, and which has differing effects on juveniles and adults, as described below.

All rabbits undergo age and sex-specific mortality, which is expressed as probability of survival over a given time period. The user-defined survival rates refer to annual survival for adults, survival to 6 months for juveniles, and survival to the 21-day nestling period for infants. The model actually translates this into a number of survival periods: thus adults face a probability of death once a month, juveniles once 2 weeks, with infants undergoing a daily survival probability. The survival probabilities for these time periods are derived from the user-defined values as follows: if p is the probability of survival over time t, such that:

$$N_{t+1} = pN_t, \tag{7}$$

then q, the probability of survival over each of x equal subdivisions of t can be derived as:

$$q = p^{1/x}, \tag{8}$$

where $q > p$. Survival to time $t + x$ is thus:

$$N_{t+x} = qN_t, \tag{9}$$

and

$$N_{t+1} = qN_t, qN_{t+x}, qN_{t+2x}, \ldots, qN_{(t+1)-x}. \tag{10}$$

Although the daily probability of survival will vary during these time periods, due to presence of predators, climatic events etc. the survival probabilities can be seen as the mean probability of survival for that period. Rabbits that die are removed from the model completely. The model tracks deaths from natural causes, extra mortality and disease separately. Natural mortality occurs at the same rate irrespective of the disease status of an individual.

2.1.5. Additional interactions and mortality

If a rabbit does not interact with another rabbit for more than 10 days, it will move to another warren. This is to avoid single rabbits occupying a warren, and to ensure that rabbits will congregate when at low density. As the mortality rate described above is fixed throughout the lifetime of the model, an additional period of mortality (but not due to RVHD) can be specified. This can be used to simulate a period of hunting, heavy non-human predation, or to separate the effects of myxomatosis from background mortality. For this extra period of mortality, the user supplied a start and end and mortality frequency (i.e. 'x'). This extra mortality is then calculated in exactly the same way as for normal mortality. As myxomatosis in Europe generally occurs in an annual cycle, peaking in late summer/autumn (Bell and Webb, 1991; Webb, 1993), this method was used to represent the different mortality rates experienced at different times of the year.

2.1.6. Additional mortality due to disease

Disease can be introduced into the population at any time of year, and at any point in the grid. Up to 15 rabbits in any one warren can be infected simultaneously, and more than one warren can be infected at one time. Outbreaks can occur on up to 15 separate days, at any time from the start of the run until 10 days before the end. For statistical purposes, outbreaks are only treated separately if there are no infected rabbits when infection is introduced.

Once a rabbit is infected, it is infectious until it either recovers or dies. The rabbit faces some probability of death on each day while it is infected, the probability varying according to length of time since infection. All rabbits survive 1 day, which represents the incubation period. Thereafter, there are four stages, each with its own probability of death. These stages cover days 2, 3, 4–6 and 7–13 from infection. Any rabbit that reaches 14 days from infection recovers. The user sets the probability of death at each stage, and all can vary from 0–1 inclusive (Xu and Chen, 1989). Infection of rabbits occurs when susceptible rabbits are in the same square as an infected rabbit. The main method of transmission has been demonstrated as direct contact with infected rabbits (Xu and Chen, 1989), although indirect transmission is possible. The user sets the probability of transmission of the disease. Rabbits less than 60 days old are not susceptible (Xu and Chen, 1989; Rodák et al., 1990b), and once a rabbit has recovered, it remains immune.

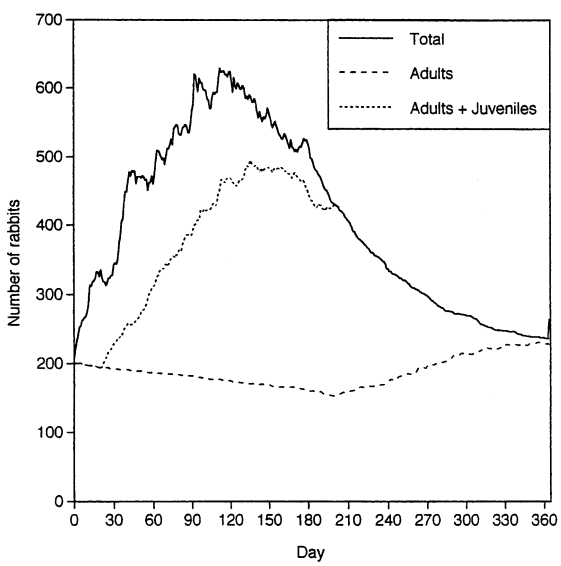

Fig. 1. Normal population development in Spatial Model.

2.2. The Spatial Model: results

The population model provided a good approximation of known rabbit population dynamics. Fig. 1 shows the annual cycle of reproduction, with breeding occurring from January through to June, followed by a period of massive juvenile mortality. This gives a relatively low level of juvenile recruitment into the adult population the following year. The figures for fecundity and recruitment matched published values closely. In Europe, the mean number of young produced per female per year has been variously reported as 6.1–10.1 (Bell and Webb, 1991 for emergent young in a UK study), 10–20 (Smith and Trout, 1994 for UK, live births) and 9.8–17.4 (Rogers et al., 1994 for France, live births). The values produced by the model varied from 9.0–18.3 births per female, which is clearly in the range reported. Likewise, Bell and Webb (1991) reported values of 8.3–51.4% for recruitment of juveniles into the adult population in a UK rabbit population, compared to values of 3.5–42.0% produced by the model.

Fig. 2 shows the effects of population density and fecundity on population growth. Fast and slow refer to the birth rate—with greater fecundity, population growth is faster. Note the clear density-dependent effect. This is not due to adult density, but rather to the decreased fecundity incurred when the total population approaches the carrying capacity of the system. With a small initial population, the full potential of births can be achieved, giving a large juvenile population from which recruitment is more successful. With a larger initial population, the carrying capacity of the system is reached with fewer births. The result is decreased production (via for example, resorption of embryos which occurs at high densities) leading to a smaller juvenile population which after mortality leaves few individuals to recruit

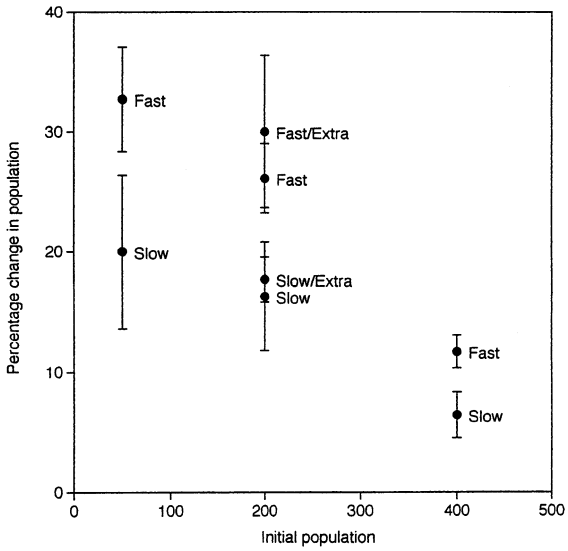

Fig. 2. Density dependence of population growth in Spatial Model.

into the adult population. When the period of high juvenile mortality (normally due to the incidence of myxomatosis) is explicitly modeled, as in the runs marked Extra in Fig. 2, there is a slight but not significant, increase in the population. This is due to the lower background mortality of juveniles which survive the extra mortality period, thus having a higher chance of surviving to become adults.

The rate of population growth is dependent upon the mean number of births per adult female (Fig. 3a). Whether the reduction in number of births per female is due to lower fecundity or for example, to increased competition for nest-sites (Bell, 1983) because of overcrowding, the result is the same—a lower rate of population increase. Dwyer et al. (1990) did not include density-dependence in their model, claiming there was a lack of evidence for this in rabbits, as has also been claimed by Gilbert et al. (1987) and Gibb (1977). However, Krebs (1986) points out that many studies have ignored the effect of social behavior on population regulation, and suggests that some self-regulation must exist in rabbits. The phenomenon of resorption of fetuses in crowded warrens (Thompson and Worden, 1956; Lockley, 1964) provides a mechanism for natural regulation of population size in rabbits. The model operates in the way that this mechanism suggests, by reducing fecundity at high population densities.

The model did not, however, allow for increased mortality at a number of disease scenarios to be investigated. Disease showed density-dependent effects (Fig. 3b), with a much larger decrease in population observed with larger initial populations. This is due to the greater number of susceptible rabbits available to be infected in a larger population. The change in population was strongly correlated with the number of rabbits infected (Fig. 3c), regardless of the type of disease and initial population size.

An interesting feature was the effect of virulence of the virus (in terms of both case mortality and time to death). For this investigation, High virulence was defined as producing a high case mortality within the first 2 days, with animals surviving longer than that having a high probability of recovery. Overall recovery from high virulence infection was around 15%. Low virulence followed the same time course as High virulence, but with much lower case mortality in the first 2 days. Overall recovery rate here was around 30%.

Delayed mortality produced a high case mortality, but with a much longer time to death and probability of death remaining high for 2 weeks. Recovery rate was around 15% in this case. Mixed mortality produced some mortality in the first 2 days, with a high mortality after 2 weeks, recovery being around 10%. While both High and Low virulence did on occasion produce a crash in population, often they did not do so. Delayed and Mixed virulence mortality, on the other hand, always induced a population crash, and produced a greater decrease in population than either High or Low virulence (Fig. 4a). Fig. 4b shows the effect of a Delayed virulence virus, introduced early in the year, on an initial population of 200 rabbits. Comparing this graph with Fig. 1 shows the dramatically reduced population, which is due to the mortality of adults early in the year; this reduces the number of young born and thus the potential for juveniles to be recruited to the adult population of the following

year. Juvenile mortality occurs as normal in summer/autumn.

The time of disease introduction was also an important variable influencing the size of population reduction due to disease (Fig. 4c). This was due to the increased number of susceptible rabbits available for infection, both because of the larger population size later in the year, and because of infants losing their immunity as they mature, thus adding to the number of susceptibles. This has interesting consequences when possible interactions between RVHD and myxomatosis are considered. If RVHD occurs later in the autumn, one might predict higher overall mortality within a population. This is due to the additive effects of myxomatosis (on susceptible young of the year), and RVHD on adults and juveniles recovered from myxomatosis since they would have lost their earlier kitten immunity.

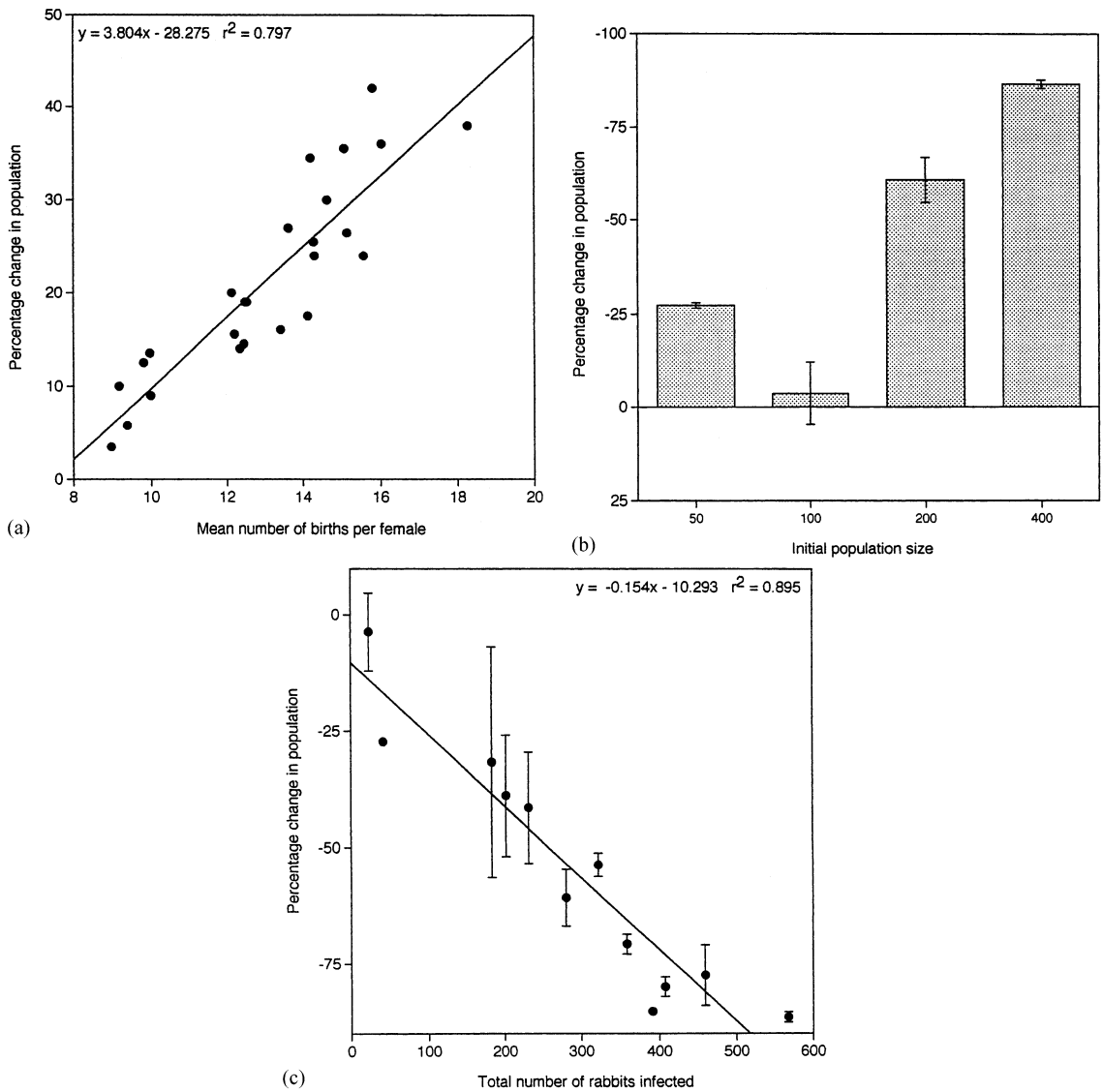

Fig. 3. (a) Effect of fecundity on population growth in Spatial Model; (b) density dependence of disease in Spatial Model; (c) effect of disease on population growth in Spatial Model.

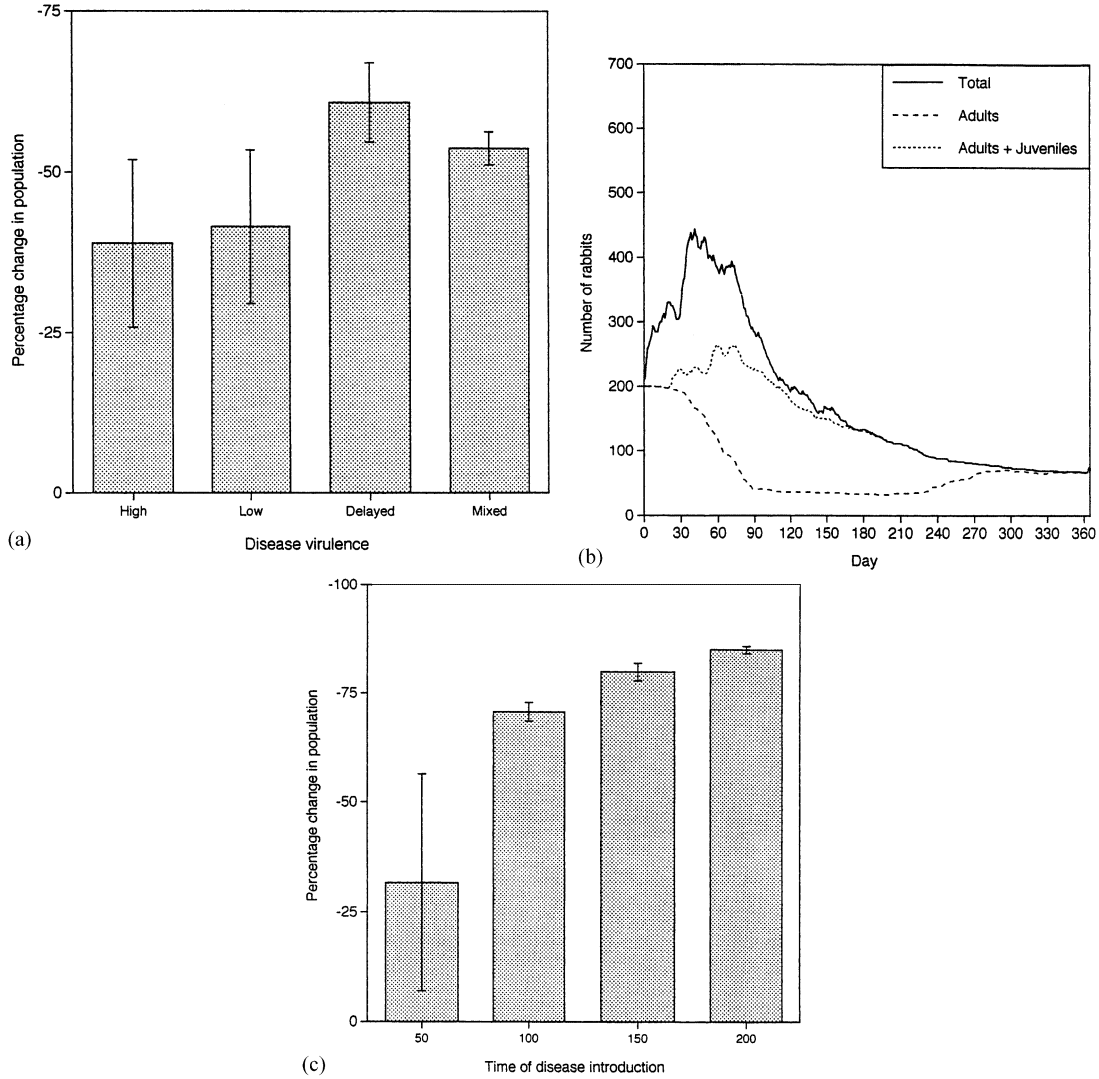

Fig. 4. (a) Effect of virulence of disease in Spatial Model; (b) population development with disease in Spatial Model; (c) effect of timing of disease in Spatial Model.

The potential for recovery in a disease-affected population is shown in Fig. 5. This population has been reduced by disease infection in November–December, from 250 rabbits in October to around 50 rabbits in January. Disease is unlikely to affect the population in the year following the first outbreak, due both to the small population size (Fig. 5a) and the low proportion of susceptible rabbits in the population (Fig. 5b). The population does not increase greatly during the year, which may be an effect of the relatively young age structure, as most of the adults in the population will be juveniles of the previous year.

2.3. The regional model: development

2.3.1. General

The Regional Model was developed from the Spatial Model, to extend the scale to several square kilometers, and several hundred thousand rabbits. This model does not explicitly represent individual rabbits but instead uses the principles

of the Spatial Model to build up a more conventional model, from which properties can be derived in terms of dynamic equations, allowing a more conventional approach. Much of the notation and variables remain the same, and the program for the Regional Model was mainly derived from that for the Spatial Model, and functions in a similar manner.

The model represents an area of 25 km^2, in a 10×10 grid of 0.25 km^2 grid-squares. Each grid-square can hold a maximum of 5000 rabbits, although the carrying capacity of each square can be set randomly at any value up to this maximum. Population processes apply to each grid-square independently; adult rabbits remain in 1 square, while juveniles may disperse between squares at certain times of the year. Each time step represents 1 week, and the model can run for up to 20 years. Most of the parameters are the same as those used in the Spatial Model (Table 2).

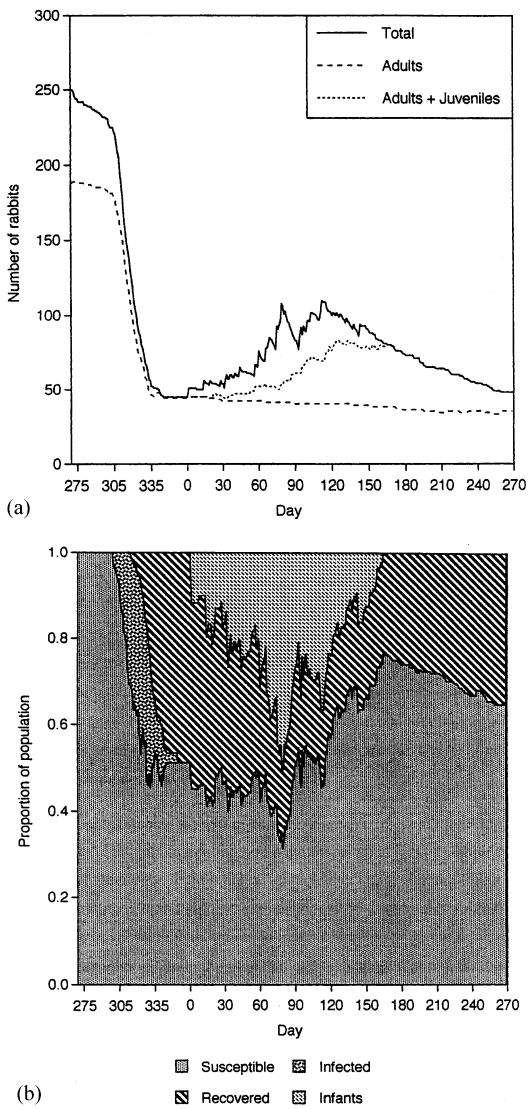

Fig. 5. (a) Recovery from disease in Spatial Model; (b) disease status during recovery in Spatial Model.

2.3.2. Individual representation

Individuals are not represented explicitly. In each grid-square, a note is kept of the total number and number of susceptible, infected and recovered rabbits in each of the five mutually-exclusive age–sex classes used in the Spatial Model. The only difference in the age/sex classes is that infants are recorded separately for each weekly cohort. This is to allow for specific mortality rates to be applied to each cohort.

2.3.3. Dispersal

Dispersal occurs in the 1st week of August each year, and is density independent and deterministic. The proportion of infants eventually dispersing is set by the user, males and females having separate rates. For each grid-square the number of dispersing juveniles is calculated, and divided equally among the eight neighboring squares. For each square it is assumed that an equal number of juveniles immigrate, and rabbits from these squares effectively only emigrate to other squares inside the model area. The number of susceptible, infected and recovered rabbits among the emigrants is proportional to the number of each of these classes within the appropriate age/sex class. Computational difficulties prevented a more realistic representation of emigration, as a number of different cohorts of juveniles would have had to be created to allow for age-related dispersion.

2.3.4. Reproduction

The number of births each month is calculated from the probability of pregnancy for that month times the number of adult females in the square times the mean litter size, adjusted by a stochastic element. The probability of pregnancy is density-

dependent so that the probability approaches zero as the square's population approaches its carrying capacity. Once the number of births for the month has been determined, the births are split into 4 weekly cohorts, in the proportion 4:3:3:2. These cohorts are then 'born' at the appropriate week of the month, only being included in the number of infants once they have been born. This allows each cohort to undergo infant mortality separately.

2.3.5. Natural mortality

Natural mortality is calculated in a similar way to that in the Spatial Model. The user supplies probabilities of survival for each age/sex class: survival to 3 weeks for infants, to 6 months for juveniles and survival over 1 year for adults. Infant mortality is calculated separately from the other age/sex class, and separately for each weekly cohort. For the remaining age/sex classes, mortality is calculated once a month, although the deaths for 1 month are spread evenly over the weeks of the month. The number of deaths in each month is calculated as the user-supplied, age/sex specific mortality rate times the number of rabbits in the age/sex class, adjusted by a stochastic element. The number of deaths in each of the disease classes is proportional to the total number of rabbits in that class for that age/sex class. Natural mortality occurs at the same rate irrespective of disease status.

2.3.6. Additional mortality due to disease

Outbreaks of the disease occur in much the same way as in the Spatial Model. The disease can be introduced in any grid-square, at any time of year, in any year of the model run. Any number of rabbits can be infected in the grid-square where disease is introduced.

Infected rabbits either recover or die, with user-defined probabilities: the sum of these two probabilities cannot exceed 1, but can be less than 1. In this latter case, rabbits that do not recover or die remain infected until the next time step. Two probabilities, TransProb and TransSquareprob govern infection of rabbits. These probabilities can be said to represent the probability of interacting with infected rabbits in the same square and in neighboring squares, respectively.

2.4. The regional model: results

The Regional Model also shows the annual population cycle seen in the Spatial Model. With the default population parameters, the maximum (adult) population achievable is around 200,000. This population size is reached regardless of the initial population size (Fig. 6a): the potential for increase in population is density dependent (Fig. 6b). The actual size of the maximum population which can be reached is dependent on the population parameters, however (Fig. 6a). A higher birth rate and low juvenile mortality allow a larger maximum population size. Paradoxically, very high juvenile mortality (80% as opposed to 70 or 60%) results in a larger population. When the population is close to carrying capacity, population growth is restricted because there are fewer births. With higher juvenile mortality there are potentially more births, as the deaths of juveniles bring the population below the carrying capacity. More births mean a larger juvenile population from which recruitment can occur, which would compensate for the increased mortality.

Three disease parameters were investigated: between-squares probability of disease transmission; virulence of disease; and frequency of occurrence of the disease (Fig. 7). It can be seen that occurrence of the disease over the 20 years was greatest with Mixed virulence disease and High between-squares probability of transmission occurring in a biennial cycle. Between-squares probability of transmission had a greater effect on occurrence of disease than either of the other two parameters. Only when this probability exceeded 0.4 (i.e. High) did a population crash occur across the entire area (Fig. 8). In the other cases, individual squares would crash completely but the disease would not transmit across the entire area. With Low between-squares probability, a maximum of 18% of squares would be infected in any 1 year, while for Medium between-squares probability, the maximum number of squares infected was 34%.

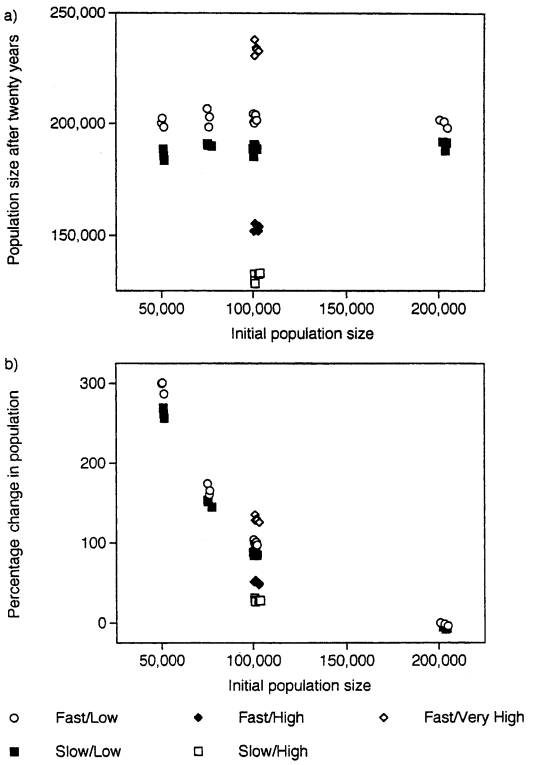

Fig. 6. Population growth in Regional Model. (a) Population size after 20 years. Note that irrespective of initial population size, the final population depends on the population parameters. (b) Density dependence of population growth. Fast and Slow refer to rate of increase, High, Very High and Low refer to juvenile mortality. The default values are: initial population of 1000, Fast rate of increase, Low mortality.

High (Fig. 8a) and Mixed (Fig. 8b) virulence disease both produced greater crashes than Low (Fig. 8c) virulence, but with low virulence a second crash occurs within the 20 years. A biennial cycle of disease also produces a second crash, but with a greater interval between the crashes. This appears to be a function of density dependence of the disease: the disease will only produce a crash once the population has reached a certain level. Low virulence produces a lower crash, so the population returns to the critical size much more quickly. Likewise, when the disease occurs in a biennial cycle, the population recovers more quickly. Mixed and High virulence disease, on the other hand, slows down the recovery. Even when the between-squares probability of transmission does not allow a crash, the disease does have a marked effect on population growth, as can be seen by comparison with the growth of population in the absence of disease in Fig. 8, solid lines.

The Regional Model represents the population in a number of grid-squares, each of which represents a discrete population, which has limited interchange with its neighboring populations. The only actual exchange of rabbits between neighboring squares is via emigrating juveniles. Thus the between-squares probability of disease transmission represents the probability that the disease will be transferred from 1 square to another. Whether this occurs by infected rabbits crossing over into another square or by an agent or vector is immaterial for the working of the model. External agents (e.g. other animals, vehicles, etc.) are reported to carry the virus, and rabbits can contract the disease from these sources (Chasey, 1994). The highest value used for the between-squares probability was 0.4. In the real world, this would require either significant movement of rabbits between populations, or a large volume of external traffic carrying the virus. It is possible that these circumstances could occur. However,

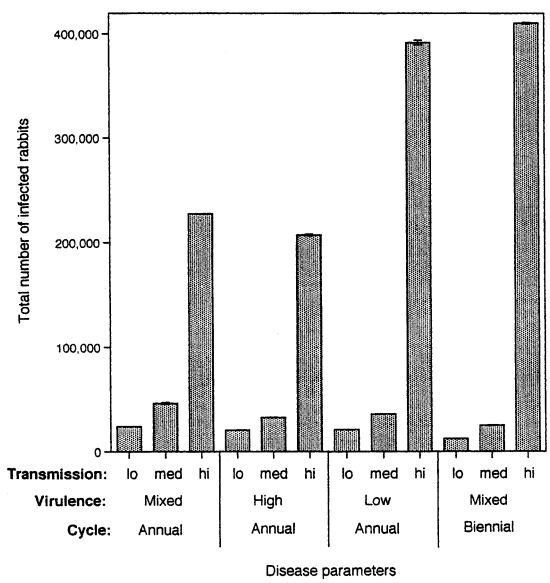

Fig. 7. Effect of disease type on number of infections in Regional Model. The disease parameters vary in probability of transmission of disease between squares (Transmission), virulence of disease (Virulence), and frequency of recurrence of disease (Cycle). Mean numbers of infected rabbits ($\pm$ standard error) for each disease type are shown.

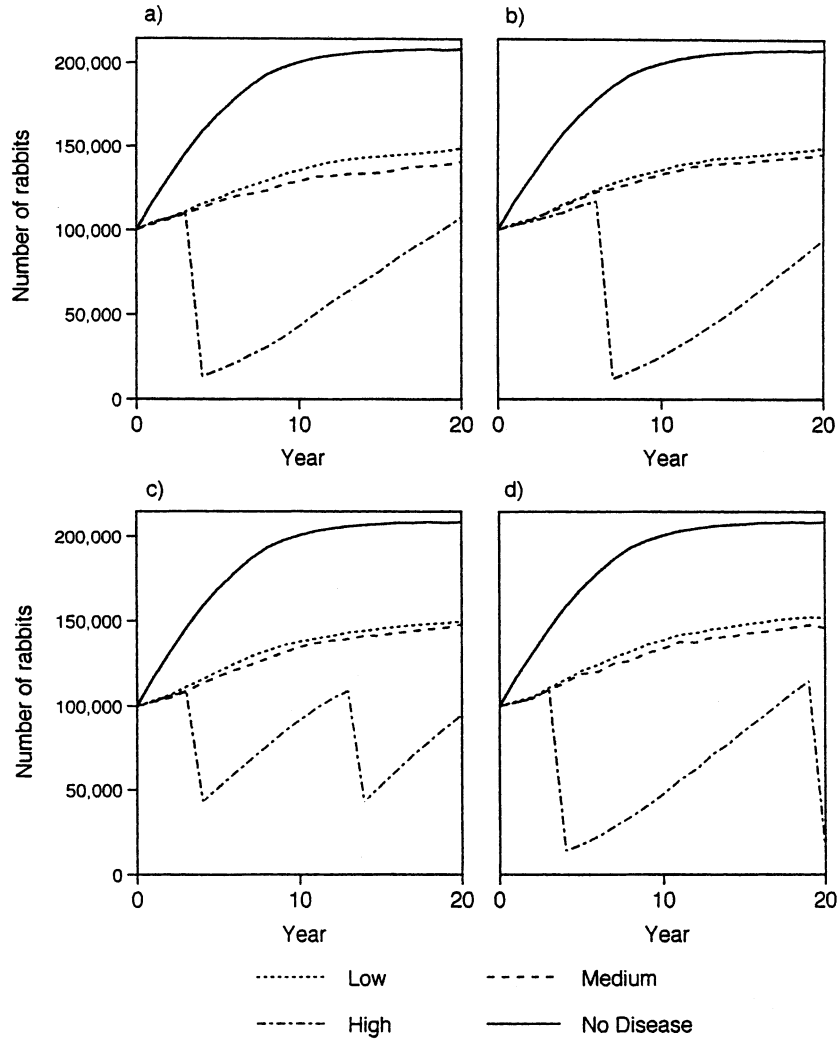

Fig. 8. Effect of disease transmissibility in Regional Model: (a) annual cycle of disease, mixed virulence; (b) annual cycle of disease, high virulence; (c) annual cycle of disease, low virulence; (d) biennial cycle of disease, mixed virulence.

the splitting of the model population into squares like this does impose some artificiality on the system. Of course, real rabbit populations are unlikely to be continuous and homogenous over an area of 25 km^2, which is why the system of grid-squares was adopted. This allows the model to simulate a system of sub-populations, representing a series of habitat patches, for example. Interactions within a patch would be relatively homogeneous, but interactions between patches would be limited.

3. Discussion

The overriding factor in considering the performance of the models is the lack of concrete data on the epidemiology of RVHD in European wild rabbits. This means that the results produced by the models cannot be extensively tested against known data. However, the underlying assumptions and limitations of the models and the effect of these on the validity and scope of the models can be discussed.

The individual-based Spatial Model produced a reasonably accurate simulation of rabbit population dynamics. However, there were some simplifications in the representation of rabbit dynamics. Mortality rates were constant throughout the year, except when extra mortality was used. The probability of natural mortality was not affected by infection with the disease. RVHD was considered to have been less likely than myxomatosis to affect this probability. Rabbits with myxomatosis have considerably altered behavior and are handicapped by impairment of vision, hearing and smell. Rabbits with RVHD do not show such a drastic alteration of behavior except in the very latest stages of the disease, which may last only a few hours. Rabbits with myxomatosis may therefore die from causes other than the disease (i.e. predation, starvation), while rabbits with RVHD are more likely to die from the disease itself. This is, therefore, included in the additional mortality due to disease.

Breeding was of fixed duration, although variation in annual reproduction could be modeled in different runs by providing different parameters. The age of the rabbits had no effect on breeding success, which is not the case in the real world. It is relatively easy to make the probability of pregnancy a function of age, as the age of each rabbit is known. Likewise, juvenile rabbits were prevented from breeding by setting the age at which juveniles became adults to 7 months. In fact, in Australia there are data that suggest that female rabbits are capable, under ideal conditions, of breeding from about 4 or 5 months, so young born early in the year could produce young of their own in the same season they were born (Gilbert et al., 1987). In the Spatial Model, this was not incorporated, as it is not common in Europe (Bell and Webb, 1991), so the number of young born in 1 year were related only to the number of individuals that were present at the start of the simulation. These assumptions simplified the program, but were unlikely to have a major effect on the results. Furthermore, these assumptions could be avoided by relatively straightforward additions to the program code. Such changes might marginally increase the running time of the program and the memory required.

Another limitation of the model was in the representation of movement and interaction between rabbits. Basically, each rabbit would be present in 1 square in 1 day, and would interact with all other animals in that square on the same day. This effectively splits the model on each day into a number of subsets. These subsets of rabbits are mutually exclusive, and all rabbits in a subset share the same set of interacting rabbits. Clearly this does not describe the pattern of interactions which real rabbits would experience. However, this method did allow rabbits to interact with different individuals on each day, and did provide a means for controlling the spread of disease. Again, with some changes in the program code, a better representation of interactions could be achieved.

As far as the representation of disease was concerned, the model provided a reasonable simulation of the known processes of RVHD. There were two main limitations of the Spatial Model. Firstly, the only means of transmission was direct contact between infected and susceptible rabbits, but in fact, in real populations indirect means of transmission are also possible (see Asgari et al., 1998).

Secondly, the disease was represented by a single strain, but with different rabbits reacting differently to it, according to some predefined probabilities. The probability of death is not correlated with either the means of infection, or the virus titer, both of which have been shown to affect the course of disease (Mitro and Krauss, 1993). Both of these features could be incorporated into the model with relative ease. Other transmission modes (insect vectors, humans and animals) could be introduced to move the disease between areas. Separate strains of the virus, which produce different responses could also be modeled, and individual rabbits could have a stochastic response to these strains, based on e.g. the amount of virus contracted.

The Spatial Model represents a relatively small area and a small rabbit population. This was due to the large processing requirements involved in this type of simulation. However, recent advances in programming software and hardware mean that larger models will be possible in the future.

In particular, parallel processing will allow a much larger model to be developed. This means that the Spatial Model could be increased in scale to approach that of the Regional Model, which would greatly increase its value.

The principal problem involved in the Regional Model is the representation of age/sex/disease classes. Time since infection, for example, could not be simulated with one class for infected rabbits. This meant that the full range of disease scenarios used in the Spatial Model could not be investigated without splitting the infected group into further sub-classes.

The other main limitation of the Regional Model was the replication of the model over the spatial grid. Each system of equations is taken to represent an area of 0.25 km^2, or 25 ha (i.e. just over four times the area of the Spatial Model); these equations were then replicated over a 10×10 grid. This grid can be seen as a series of habitat patches each with its own system of population and dynamics. Although the carrying capacity of each grid-square could be altered, the underlying dynamics (mortality, fecundity etc.) could not be changed. This could have been altered either by supplying different parameters for each grid-square, or by allowing stochastic variation in these parameters between squares.

The separation of the area into grid-squares does pose some problems, as discussed above. This lies chiefly in the parameter which controls the transmission of the disease between grid-squares; it is difficult to assess whether the values used for this parameter reflect the real world situation. This parameter expressed as a probability, shows up one of the main disadvantages of the Regional Model. The between-squares probability of transmission of disease could be defined as the probability of infected rabbits from 1 square coming into contact with susceptible rabbits in another square, or as the probability of an external agent carrying the disease across a square boundary. Both of these definitions depend on factors which are not explicitly included in the model: in the first case, the factors are the distance between squares, and the amount of movement between squares, which are not covered elsewhere, whilst in the latter case, the factor is, by definition, external. In the Spatial Model, these factors can be explicitly modeled; it would be more difficult to do so for the Regional Model.

Furthermore, the difference between the between-squares probability of transmission and the within-square probability of transmission lies in the scope of their actions. For each grid-square, the within-square probability determines the outcome of disease. For the whole area between-square probability is more important. Individual populations may crash completely due to the disease spreading throughout that square, but unless the between-squares probability crosses some threshold (0.4), the disease will not spread to all the squares in the area. Thus the spread of disease in the Regional Model is dependent on a factor which is not satisfactorily defined.

With the Spatial Model, the probability of transmission of the disease between rabbits would be the same across the whole area. The spread of the disease would be determined by the actual distance between groups of rabbits and by the movements of other agents, both of which could be modeled and controlled explicitly. This would provide a more realistic simulation of the disease, and would allow assessment of the relative importance of direct and indirect sources of transmission of the disease.

The results of this study suggest that while traditional analytical models of RVHD may provide a certain theoretical insight into the behavior of the disease in wild rabbit populations, IBMs have many advantages, which make them more useful. The IBM described here will, however, have to be developed in a number of respects for full utilization of those advantages. Changing the way that rabbits are located in space can incorporate better representation of movement and interaction. For example, each rabbit has a set of other rabbits with which it interacts, and this set will not necessarily be the same for any other rabbit. Interactions could be further influenced both by the age/sex class and the dominance status of the rabbit. Other ways in which the Spatial Model can be improved are in the representation of breeding behavior, further separation of natural mortality causes, larger scale and separation of the virus into strains. As discussed

above, these changes can all be incorporated with straightforward alterations to the program code.

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